Atty Dkt. No. 027668/0106

U.S. PATENT APPLICATION

for

Apparatus and Methods for Delivering a Plurality of Medicaments for Management of Co-Morbid Diseases, Illnesses or Conditions

Inventors: Frederick H. Miller

Apparatus and Methods for Delivering a Plurality of Medicaments for Management of Co-Morbid Diseases, Illnesses or Conditions

CROSS-REFERENCE TO RELATED PATENT APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application Serial Number 60/451,150, entitled Apparatus and Methods for Delivering a Plurality of Medicaments for Management of Co-Morbid Diseases, Illnesses or Conditions, filed on February 27, 2003, the contents of which are incorporated by reference herein in their entirety. This application also claims priority to U.S. Provisional Patent Application Serial Number 60/450,615, filed on February 27, 2003, entitled, Apparatus and Methods for Delivering a Plurality of Medicaments for Management of a Disease, Illness or Condition Affecting One or More Organ Systems the contents of which are incorporated by reference herein in their entirety. This application is related to U.S. Patent Application Serial Number _____, filed on February 26, 2004, entitled, Apparatus and Methods for Delivering a Plurality of Medicaments for Management of a Disease, Illness or Condition Affecting One or More Organ Systems, identifying Frederick H. Miller as the inventor, the contents of which are incorporated by reference herein in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to methods for the administration of a plurality of heterogenous chemical and biological compounds to animals and humans using a multi-compartment delivery system for treatment of separate conditions or diseases in one or more organ systems.

BACKGROUND OF THE INVENTION

[0003] Administration of chemicals and biomolecules to animals and humans may first appear to be a simple undertaking, however, the contemplation, design, testing, and manufacture of elegant pharmaceutical products requires a thorough integration of medical and pharmacy principles.

[0004] The art and practice of pharmacy can be divided into four distinct divisions. Pharmacology is the study of interactions occurring between the pharmacologic agent, or medicament and specific targeted cells in the body. More specifically, the interaction between an active agent and a cellular receptor along with the resulting change in cell physiology is examined. Medicinal chemistry is largely concerned with the identification of naturally occurring and synthetic compounds which possess medicinal characteristics. Pharmacotherapeutics is the holistic application of pharmacy practice to specific pathologies, illnesses, and other body functions. Finally, Pharmaceutical science ascertains or regulates the composition of medicinal substances, and is largely directed to the development of new mechanisms for delivering chemicals and biomolecules into animals and humans. A sub-category of pharmaceutical science is called pharmacokinetics and sometimes generally referred to as biopharmaceutics.

[0005] A.D.M.E. is an acronym often used to describe the four essential components to pharmaceutical science: absorption, distribution, metabolism, and elimination, respectively. One way to differentiate between pharmacology and pharmaceutical science is that the former is primarily concerned with the effect of the medicament on the body, whereas, the latter is primarily concerned with the delivery and time-course of the medicament on its journey through the body.

[0006] In clinical applications, chemicals and biomolecules are often referred to as active ingredients or medicaments. Medicaments may include "pharmaceuticals, nutraceuticals, biotechnicals, vitamins, minerals and dietary supplements." Oral

administration is the most frequent route for delivery of medicaments. Medicaments may be orally administered in a variety of physical states, including, solid, liquid, dispersion, and gaseous forms. As appreciated, tablets and capsules are the most common vehicle for oral delivery of medicaments.

[0007] Frequently, a medical or surgical patient may receive a plurality of concurrent medicaments. Data has been accumulated to demonstrate that patients undergoing a surgical procedure may receive ten (10) or more medicaments during the surgery and the resulting surgical recovery period. Some patients who have undergone organ transplantation or who have contracted human immunodeficiency virus (HIV) may receive three (3) or more medicaments which require multiple administrations per day. HIV patients often receive many more than three (3) medicaments. These medicaments may be necessary for the treatment of several conditions occurring in a plurality of organ systems or they may be necessary to treat a single condition or some combination thereof.

[0008] In some cases, it may be desirous to combine a plurality of medicaments because of a synergistic interaction between a plurality of medicaments. This synergy may enhance the efficacy of one or more of the medicaments. Medicaments may be combined to increase the intensity of response or efficacy. A plurality of medicaments, in combination, may be homergic (*i.e.*, ellicit the same quality of effect). In many cases, a plurality of homergic medicaments may also be homodynamic (*i.e.*, interact with the same receptor). A plurality of homergic medicaments may be additive, supra-additive and infra-additive. A plurality of combined medicaments which do not produce the same quality of response may be called, heterergic. When heterergy is found to be a positive effect (*i.e.*, at least one medicament enhances the response to another medicament), this may be called synergism and is sometimes called synergy.

[0009] In further cases, it may be desirous to combine a plurality of medicaments to decrease their individual dosages and possibility for toxicity. It may also be desirous to combine a plurality of medicaments to target the treatment of a disease, illness or

condition from divergent angles. It may be desirous to combine a plurality of medicaments to minimize the side effects and adverse effects of one or more medicaments. It may be still further desirous to combine a plurality of medicaments to alter the pharmacokinetic characteristics of one or more medicaments. For example, alterations in the absorption, distribution, metabolism or elimination of one or more medicaments.

[0010] Fixed combinations of a plurality of medicaments have been generally disfavored due to any number of perceived disadvantages. These disadvantages may include, for example: (1) complicating the interpretation of safety and efficacy in therapeutic regimens, (2) there may be inter-patient differences to fixed combinations, (3) there may be difficulties in dosage titration, and (4) the delivery platforms for fixed combinations have generally been found to be uneconomical to produce.

[0011] On the other hand, fixed combinations of a plurality of medicaments may lead to several therapeutic advantages, including, for example, but not by way of limitation: (1) increasing patient compliance with therapy, (2) increasing efficacy by optimizing timing of medicaments, (3) minimization of side effects and adverse effects, (4) enhancement of pharmacokinetic characteristics of one or more medicaments in a fixed combination, (5) increased patient quality of life, (6) optimization of institutional resources by minimizing the amount of medicament administrations, and (7) minimizing patient length of stay in institutional facilities by optimizing therapy.

[0012] Prior art therapeutic technologies contain isolated examples of pharmaceutical formulations containing fixed combinations of medicaments. However, therapeutic technologies of the prior art teach a fixed combination, wherein a plurality of medicaments are placed into a single receiving chamber in the delivery formulation (*i.e.*, no separation between the plurality of medicaments). In addition, those skilled in the art developed therapeutic technologies that contemplate the use of a multi-compartment (*i.e.*,

multiple-receiving chambered) delivery vehicle for treating *helicobacter pylori*-induced peptic ulcer disease.

[0013] In view of the state of the technology as it exists today, generally, therapeutic apparatus and methods are needed to provide a plurality of medicaments for medical and surgical conditions, as well as maintenance of normal health function for delivery to animals and humans using a multi-chambered delivery apparatus. Such apparatus and methods for delivering a plurality of medicaments to animals and humans using a multi-chambered delivery apparatus are contemplated herein.

SUMMARY OF THE INVENTION

[0014] A primary object of the present invention is to provide novel delivery apparatus and methods for affecting multiple organ systems in animals or humans using a plurality of medicaments delivered by a pharmaceutical formulation comprising a multi-chambered apparatus. Accordingly, the present invention provides novel delivery apparatus and administration techniques or methods aimed at affecting multiple organ systems in an animal or human using a plurality of medicaments. A delivery apparatus may be in any multi-chambered apparatus, but preferably in a capsular formulation. Thus, a plurality of medicaments may be encapsulated and stored separately within a larger capsule until the time of ingestion, consumption, or the like. Upon consumption, the capsule walls of one or more dividing walls of a capsule may dissolve to release their contents. Different methods of encapsulation may be used to deliver their respective contents, including but not limited to, dissolution, melting, ablation or biodegradation of the encapsulating wall. In certain embodiments and as contemplated herein, the medicaments retained in the multi-compartment capsule may actually diffuse through one or more of the encapsulating walls.

[0015] In accordance with one presently preferred embodiment of the present invention, an encapsulated product may be provided in several parts, including a primary

capsule and one or more secondary capsules enclosed therein. In other presently preferred embodiments, a capsule may be provided having separate compartments or sections where ingredients may be stored and released at desired time intervals. More specifically, a process for encapsulating secondary smaller capsules in a larger primary capsule is contemplated hereinbelow. In one presently preferred embodiment, a process in accordance with the present invention may include the steps of:

1. Providing a primary capsule with a receiving chamber, wherein, in certain preferred embodiments, the primary capsule may be provided in two parts, such as a body portion and a cap portion, which may be sealed together to retain ingredients contained therein;

2. Providing one or more secondary capsules having a dimensional size sufficient so that medicaments and the secondary capsule may be introduced within the receiving chamber of the primary capsule, wherein, in selected preferred embodiments, the secondary capsule may also be provided in two parts, such as a body portion and a cap portion, which may be sealed together to retain ingredients contained therein;

3. Filling the receiving chamber of a secondary capsule with one or more medicaments, wherein said medicaments may be the same or different from medicaments in other receiving chambers;

4. Sealing one or more medicaments within the secondary capsule;

5. Inserting the secondary capsule into at least a portion of the receiving chamber of the primary capsule;

6. Filling the body portion of the primary capsule, housing one or more secondary filled capsules, with one or more medicaments; and

7. Sealing one or more medicaments and one or more secondary capsules within a receiving chamber of the primary capsule.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] The objects and features of the present invention will become more fully apparent from the following description, taken in conjunction with the accompanying drawings and appendicies. Understanding that the Figures depict presently preferred embodiments of the present invention and are, therefore, not to be considered limiting of its scope, the invention will be described with additional specificity and detail through use of the accompanying drawings and appendicies in which:

[0017] Fig. 1 is flow chart illustrating several preferred embodiments of the present invention, wherein said embodiments originating from five (5) proprietary products belonging to Pfizer, Incorporated;

[0018] Fig. 2 is flow chart illustrating several preferred embodiments of the present invention, wherein said embodiments originating from five (5) proprietary products belonging to Glaxo SmithKline, P.L.C;

[0019] Fig. 3 is flow chart illustrating several preferred embodiments of the present invention, wherein said embodiments originating from five (5) proprietary products belonging to Merck & Co;

[0020] Fig. 4 is flow chart illustrating several preferred embodiments of the present invention, wherein said embodiments originating from five (5) proprietary products belonging to AstraZeneca, P.L.C; and

[0021] Fig. 5 is flow chart illustrating several preferred embodiments of the present invention, wherein said embodiments originating from five (5) proprietary products belonging to Novartis, Incorporated.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0022] It will be readily understood that the components of the present invention as detailed below, may be arranged and designed in a wide variety of different configurations and steps. Thus, the description herein is not intended to limit the scope of the invention, but is merely representative of certain presently preferred embodiments in accordance with the invention and its inherent inventive concepts. Those of ordinary skill in the art will, of course, appreciate that various modifications to the details herein may easily be made without departing from the essential characteristics of the invention, as described. Thus, the following information is intended only by way of example, and simply illustrates certain presently preferred embodiments consistent with the invention.

[0023] Appendix I contains a list of diseases, illnesses and conditions which are known to affect several organ systems and a list of medicaments which may be helpful in managing said diseases, illnesses and conditions, the contents of Appendix I being incorporated herein by reference in their entirety.

[0024] Referring to generally to Appendix I, it may be demonstrated that as medical and pharmacy knowledge has continued to expand exponentially, new medicaments, new classes of medicaments and new delivery technologies are becoming available for use in animals and humans who experience particular medical diseases, illnesses or conditions. A disease, illness, or condition may affect one or more organ systems in an animal or

human. Organ systems may include, for example: (1) autonomic, (2) cardiovascular, (3) neurological, (4) gastro-intestinal, (5) respiratory, (6) renal system, (7) psychiatric, (8) endocrine, (9) gynecologic, (10) urologic, (11) immunologic, (12) bone and joint systems, (13) ear, nose, and throat, (14) dermatologic, (15) hematologic, (16) infectious defense and (17) nutrition and metabolism. In an animal or human who may be suffering from one disease, illness or condition, it is common to also be suffering from a disease, illness or condition affecting one or more of the other organ system(s). These concomitant diseases, illnesses or conditions occurring within a single animal or human are often labeled as "co-morbidities", a term often shortened and referred to as "co-morbid."

[0025] New medicaments and delivery technologies are providing patients and their health care practitioners with unprecedented therapeutic options in managing diseases, illnesses and conditions. In spite of this sophistication, there has been no effort to develop new methods of using fixed combinations of medicaments for therapy of co-morbid diseases, illnesses or conditions. Moreover, there has been no effort to develop new methods of using fixed combinations of medicaments for management of a single disease, illness or condition affecting one or more organ system(s). The aforementioned fixed combinations may include a plurality of medicaments, which may be newly discovered and developed, or have been known for sometime or some combination of medicaments thereof. In any regard, said fixed combinations have not previously been contemplated in the art.

[0026] The following examples will illustrate the invention in further detail. It will be readily understood that the various plurality of medicaments that may be introduced into the receiving chambers of the multi-compartment vehicles of the present invention, as generally described and illustrated in the Examples herein, are to be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or process for implementing those principles. Thus, the following more detailed description of the presently preferred embodiments of the methods, formulations, and compositions

of the present invention, as represented in Examples I - V, is not intended to limit the scope of the invention, as claimed, but is merely representative of presently preferred embodiments of the invention.

EXAMPLE I

[0027] Referring to Fig. 1, in one presently preferred embodiment of the present invention, a plurality of medicaments are delivered in a single vehicle for management of co-morbid diseases, illnesses or conditions. More particularly, a plurality of medicaments comprising an HMG CoA Reductase inhibitor, for example, atorvastatin (LIPITOR® manufactured by Pfizer, Inc.), and a serotonin reuptake inhibitor, for example, sertraline (ZOLOFT® manufactured by Pfizer, Inc.), may be combined into a single delivery apparatus, for example, a multi-compartment capsule.

[0028] In the presently preferred embodiment, a therapeutically effective amount of atorvastatin (LIPITOR® manufactured by Pfizer, Inc.), may be introduced into a receiving chamber of a secondary capsule. The base and cap of the secondary capsule may then be sealed using any available conventional means readily known to those skilled in the art. The secondary capsule may then be introduced into a receiving chamber in a primary capsule. A therapeutically effective amount of sertraline (ZOLOFT® manufactured by Pfizer, Inc.) may be introduced into the receiving chamber of the primary capsule. The base and cap of the primary capsule may then be sealed using any available conventional means readily known to those skilled in the art.

[0029] A capsular format of the present invention may include the following composition:

Primary Capsule:	
sertraline (ZOLOFT® manufactured by Pfizer, Inc.)	100 mg
[dosage range 50 - 200 mg / day]	
Secondary Capsule:	
atorvastatin (LIPITOR® manufactured by Pfizer, Inc.)	20 mg
[dosage range 10 - 80 mg / day]	

[0030] The incorporation of time-release coatings to vary the release rates of the medicaments (*e.g.*, sertraline (ZOLOFT® manufactured by Pfizer, Inc.) and atorvastatin (LIPITOR® manufactured by Pfizer, Inc.)) in the primary and secondary capsules, respectively, of the multi-compartment capsule may be used to target key time intervals or events when the body may be most able to utilize the named active ingredients. For example, HMG CoA Reductase Inhibitors are known to as much as a 70% increase in efficacy when administered in the evening hours. Thus, by varying the composition of the secondary capsular wall, release of the contents of the secondary capsule may be targeted to an optimal delivery time. A differential release between the primary capsule and secondary capsule may therefore optimize management of co-morbid conditions in a patient. The patient is able to take a single daily administration vehicle, which provides a plurality of medicaments for managing co-morbid conditions. Thus, the incorporation of time-release coatings in the encapsulation process when forming a multi-compartment capsule may be specifically designed to fit the needs and desires of numerous different users having similar conditions that are being targeted for treatment. It is intended,

therefore, that the examples provided herein be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or method for implementing those principles.

EXAMPLE II

[0031] Referring to Fig. 2, in one presently preferred embodiment of the present invention, a plurality of medicaments are delivered in a single vehicle for management of co-morbid diseases, illnesses or conditions. More particularly, a plurality of medicaments comprising a thiazolidinedione derivative, for example, rosiglitazone (AVANDIA® manufactured by Glaxo SmithKline), and a serotonin reuptake inhibitor, for example, paroxetine (PAXIL® manufactured by Glaxo SmithKline) may be combined into a single delivery apparatus, for example, a multi-compartment capsule.

[0032] In the presently preferred embodiment, a therapeutically effective amount of paroxetine (PAXIL® manufactured by Glaxo SmithKline) may be introduced into a receiving chamber in a secondary capsule. The base and cap of the secondary capsule may then be sealed using any available means readily known to those skilled in the art. A therapeutically effective amount of rosiglitazone (AVANDIA® manufactured by Glaxo SmithKline) may be introduced into a receiving chamber in a primary capsule. The secondary capsule may then be introduced into a receiving chamber in a primary capsule. The primary capsule may then be sealed using any available means readily known to those skilled in the art.

[0033] A capsular format of the present invention may include the following composition:

Primary Capsule:	
rosiglitazone (AVANDIA® manufactured by Glaxo SmithKline)	4 mg
[dosage range 4 - 8 mg / day]	
Secondary Capsule:	
paroxetine (PAXIL® manufactured by Glaxo SmithKline)	20 mg
[dosage range 20 - 60 mg / day]	

[0034] The incorporation of time-release coatings to varying the release rates of the medicaments (*e.g.*, rosiglitazone (AVANDIA® manufactured by Glaxo SmithKline) and paroxetine (PAXIL® manufactured by Glaxo SmithKline)) in the primary and secondary capsules, respectively, of the multi-compartment capsule may be used to target key time intervals or events when the body may be most able to utilize the named active ingredients. For example, paroxetine (PAXIL® manufactured by Glaxo SmithKline) is known to have sedating effects similar to antihistamines. Therefore, to minimize these effects on activities of daily living, paroxetine (PAXIL® manufactured by Glaxo SmithKline) is recommended for administration in the evening hours. Thus, by varying the composition of the secondary capsule wall, release of the contents of the secondary capsule may be targeted to an optimal time. A differential release between the primary capsule and secondary capsule may therefore optimize management of co-morbid conditions in a patient. The patient is able to take a single daily administration vehicle, which provides a plurality of medicaments for managing co-morbid conditions. Thus, the incorporation of time-release coatings in the encapsulation process when forming a multi-compartment capsule may be specifically designed to fit the needs and desires of

numerous different users having similar conditions that are being targeted for treatment. It is intended, therefore, that the examples provided herein be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or method for implementing those principles.

EXAMPLE III

[0035] Referring to Fig. 3, in one presently preferred embodiment of the present invention, a plurality of medicaments are delivered in a single vehicle for management of co-morbid diseases, illnesses or conditions. More particularly, a plurality of medicaments comprising a bisphosphonate, for example, alendronate (FOSAMAX® manufactured by Merck & Co.) and an HMG CoA Reductase Inhibitor, for example, simvastatin (ZOCOR® manufactured by Merck & Co.) may be combined into a single delivery apparatus, for example, a multi-compartment capsule.

[0036] In the presently preferred embodiment, a therapeutically effective amount of simvastatin (ZOCOR® manufactured by Merck & Co.) may be introduced into a receiving chamber in a secondary capsule. The base and cap of the secondary capsule may then be sealed using any available conventional means readily known to those skilled in the art. The secondary capsule may then be introduced into a receiving chamber in a primary capsule. A therapeutically effective amount of alendronate (FOSAMAX® manufactured by Merck & Co.) may be introduced into a receiving chamber in a primary capsule. The base and cap of the primary capsule may then be sealed using any available conventional means readily known to those skilled in the art.

[0037] A capsular format of the present invention may include the following composition:

Primary Capsule:

alendronate (FOSAMAX® manufactured by Merck & Co.) 5 mg

[dosage range 5 - 10 mg / day]

Secondary Capsule:

simvastatin (ZOCOR® manufactured by Merck & Co.) 40 mg

[dosage range 5 - 80 mg / day]

[0038] The incorporation of time-release coatings to varying the release rates of the medicaments (*e.g.*, alendronate (FOSAMAX® manufactured by Merck & Co.) and simvastatin (ZOCOR® manufactured by Merck & Co.)) in the primary and secondary capsules, respectively, of the multi-compartment capsule may be used to target key time intervals or events when the body may be most able to utilize the named active ingredients. For example, HMG CoA Reductase Inhibitors are known to as much as a 70% increase in efficacy when administered in the evening hours. Therefore, to maximize its effects, simvastatin (ZOCOR® manufactured by Merck & Co.) is recommended for administration in the evening hours. Morover, alendronate (FOSAMAX® manufactured by Merck & Co.) is known to have an extremely low bioavailability following oral administration. Alendronate (FOSAMAX® manufactured by Merck & Co.) is recommended to be taken on an empty stomach upon waking in the morning. It is also recommended that the patient stay in an upright position for at least 30 minutes following administration. Therefore the presently preferred embodiment of the present invention is ideally suited for increasing patient compliance.

[0039] Thus, by varying the composition of the secondary capsule wall, release of the contents of the secondary capsule may be targeted to an optimal delivery time. A differential release between the primary capsule and secondary capsule may therefore optimize management of co-morbid conditions in a patient. The patient is able to take a single daily administration vehicle, which provides a plurality of medicaments for managing co-morbid conditions. Thus, the incorporation of time-release coatings in the encapsulation process when forming a multi-compartment capsule may be specifically designed to fit the needs and desires of numerous different users having similar conditions that are being targeted for treatment. It is intended, therefore, that the examples provided herein be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or method for implementing those principles.

EXAMPLE IV

[0040] Referring to Fig. 4, in one presently preferred embodiment of the present invention, a plurality of medicaments are delivered in a single vehicle for management of co-morbid diseases, illnesses or conditions. More particularly, a plurality of medicaments comprising a beta-adrenergic receptor antagonist, for example, metoprolol (TOPROL XL® manufactured by AstraZeneca) and a proton pump inhibitor, for example, omeprazole (PRILOSEC® manufactured by AstraZeneca) may be combined into a single delivery apparatus, for example, a multi-compartment capsule.

[0041] In the presently preferred embodiment, a therapeutically effective amount of omeprazole (PRILOSEC® manufactured by AstraZeneca) may be introduced into a receiving chamber in a secondary capsule. The base and cap of the secondary capsule may then be sealed using any available conventional means readily known to those skilled in the art. The secondary capsule may then be introduced into a receiving chamber in a primary capsule. A therapeutically effective amount of metoprolol (TOPROL XL® manufactured by AstraZeneca) may be introduced into a receiving

chamber in a primary capsule. The base and cap of the primary capsule may then be sealed using any available conventional means readily known to those skilled in the art.

[0042] A capsular format of the present invention may include the following composition:

Primary Capsule:

metoprolol (TOPROL XL®manufactured by AstraZeneca) 100 mg

[dosage range 25 - 200 mg / day]

Secondary Capsule:

omeprazole (PRILOSEC® manufactured by AstraZeneca) 20 mg

[dosage range 20 - 80 mg / day]

[0043] The incorporation of time-release coatings to varying the release rates of the medicaments (*e.g.*, metoprolol (TOPROL XL® manufactured by AstraZeneca) and omeprazole (PRILOSEC® manufactured by AstraZeneca)) in the primary and secondary capsules, respectively, of the multi-compartment capsule may be used to target key time intervals or events when the body may be most able to utilize the named active ingredients. For example, the peak acid secretion in the gastrointestinal system is believed to occur during sleep. Proton pump inhibitors may therefore be more efficacious when administered in the evening hours and thus allowing a peak systemic concentration to coincide with higher levels of acid production. Therefore, to maximize its effects, omeprazole (PRILOSEC® manufactured by AstraZeneca) is recommended for

administration in the evening hours. Therefore the presently preferred embodiment of the present invention is ideally suited for increasing patient compliance.

[0044] Thus, by varying the composition of the secondary capsule wall, release of the contents of the secondary capsule may be targeted to an optimal delivery time. A differential release between the primary capsule and secondary capsule may therefore optimize management of co-morbid conditions in a patient. The patient is able to take a single daily administration vehicle, which provides a plurality of medicaments for managing co-morbid conditions. Thus, the incorporation of time-release coatings in the encapsulation process when forming a multi-compartment capsule may be specifically designed to fit the needs and desires of numerous different users having similar conditions that are being targeted for treatment. It is intended, therefore, that the examples provided herein be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or method for implementing those principles.

EXAMPLE V

[0045] Referring to Fig. 5, in one presently preferred embodiment of the present invention, a plurality of medicaments are delivered in a single vehicle for management of co-morbid diseases, illnesses or conditions. More particularly, a plurality of medicaments comprising an acetylcholinesterase inhibitor, for example, rivastigmine (EXELON® manufactured by Novartis, A.G) and an angiotensin II receptor antagonist, for example, valasartan (DIOVAN®manufactured by Novartis, A.G) may be combined into a single delivery apparatus, for example, a multi-compartment capsule.

[0046] In the presently preferred embodiment, a therapeutically effective amount of valasartan (DIOVAN® manufactured by Novartis, A.G) may be introduced into a receiving chamber in a secondary capsule. The base and cap of the secondary capsule may then be sealed using any available conventional means readily known to those skilled in the art. The secondary capsule may then be introduced into a receiving

chamber in a primary capsule. A therapeutically effective amount of rivastigmine (EXELON® manufactured by Novartis, A.G) may be introduced into a receiving chamber in a primary capsule. The base and cap primary capsule may then be sealed using any available conventional means readily known to those skilled in the art.

[0047] A capsular format of the present invention may include the following composition:

Primary Capsule:

rivastigmine (EXELON® manufactured by Novartis, A.G) 9 mg

[dosage range 6-12 mg / day]

Secondary Capsule:

valasartan (DIOVAN®manufactured by Novartis, A.G) 120 mg

[dosage range 80 - 320 mg / day]

[0048] The incorporation of time-release coatings to varying the release rates of the medicaments (*e.g.*, rivastigmine (EXELON® manufactured by Novartis, A.G) and valasartan (DIOVAN® manufactured by Novartis, A.G)) in the primary and secondary capsules, respectively, of the multi-compartment capsule may be used to target key time intervals and optimize patient compliance. For example, rivastigmine (EXELON® manufactured by Novartis, A.G) is labeled for use in patients suffering from Alzheimer's disease, a type of dementia. These patients often have difficulty remembering tasks associated with activities of daily living. It is known that these patients may forget to take their medicines. By reducing the daily administration of medicine in this patient,

there may be improved patient compliance. Therefore the presently preferred embodiment of the present invention is ideally suited for increasing patient compliance.

[0049] Thus, by varying the composition of the secondary capsule wall, release of the contents of the secondary capsule may be targeted to an optimal time. A differential release between the primary capsule and secondary capsule may therefore optimize management of co-morbid conditions in a patient. The patient is able to take a single daily administration vehicle, which provides a plurality of medicaments for managing co-morbid conditions. Thus, the incorporation of time-release coatings in the encapsulation process when forming a multi-compartment capsule may be specifically designed to fit the needs and desires of numerous different users having similar conditions that are being targeted for treatment. It is intended, therefore, that the examples provided herein be viewed as exemplary of the principles of the present invention, and not as restrictive to a particular structure or method for implementing those principles.

[0050] As can be seen above, various embodiments of the present invention can be utilized in specific medical applications. By way of example only and not by way of limitation, the present invention can be practiced to prepare delivery devices for use in chemotherapy to address/treat, by way of example and not by limitation, the following aspects of chemotherapy: psychological, timing (to coincide with tumor growth for example) route of administration, nausea, vomiting (CINV), compliance, and cost (e.g. reduce hospital management of patients, reduce the number of "repeat" drug doses due to patient vomiting, etc.). Still futher, the just mentioned aspects are not limited to chemotherapy, as the present invention can be practiced to address common aspects between chemotherapy and other treatments.

[0051] Further by way of examples, capsules containing Zofran (ondansertron), Temodar (temozolomide) can be made.

[0052] Still further, the present invention can be used in cardiovascular treatments, for example hypertension, heart failure, and heart rhythm disorders. Also, the present invention can be used in immunology (e.g. transplant rejections, auto-immune disorders, etc.). The present invention can be used to treat neurological disorders (such as Parkinson's disease, dementia, stroke, epilepsy, and migraine headache, etc.), psychiatric disorders (schizophrenia, bipolar disease, depression, anxiety, ADHD / ADD, Addictions, etc.), infectious diseases (fungal, bacterial, viral (HIV), etc.), and in anesthesiology (induction anesthesia, local anesthesia). Furthermore, the present invention has application in endocrinology (cholesterol, diabetes, hormone replacement therapy, thyroid dysfunction, oral contraception, obesity, etc.), dermatology (onychomycosis, acne, rosaceae, psoriasis, etc.), rheumatology (arthritis, gout, osteoporosis / Osteomalacia), respiratory fields (asthma, emphysema, cystic fibrosis, etc.), gastro-intestinal fields (gastro-esophageal reflux disease, ulcer prophylaxis, crohn's disease, inflammatory bowel disease, etc.), chronic renal failure (vitamin and mineral replacement, blood pressure regulation, diabetes, depression, etc.), genito-urinary (enlarged prostate / BPH, overactive bladder, erectile dysfunction, feminine yeast infections, etc.) and hematology-oncology (thromboembolous, hermatopoeisis, neoplastic disease, nausea / vomiting).

[0053] The present invention may be utilized for dual / multiple disease state therapy with one capsule, dual / multiple organ system therapy with one capsule, enhanced pharmacoeconomic delivery, temporal / circadian optimized delivery, sports nutrition, sports therapy, athletic performance enhancement and law enforcement and military applications.

[0054] The present invention may be embodied in other specific forms without departing from its spirit or essential characteristics. The described embodiments are to be considered in all respects only as illustrative, and not restrictive. One skilled in the art will recognize that this technology may be applicable for providing a wide variety a

plurality of medicaments in a single delivery vehicle for management of co-morbid diseases, illnesses or conditions.

[0055] Other drugs that may be combined, into a single delivery apparatus, for example, a multi-compartment capsule, according to the present invention include, by way of example, Lipitor (by Pfizer), Prilosec (by Astra Zenica), Prevacid (by Tap), Zocor (by Merck), Celebrex (by Searle), Zoloft (by Pfizer), Paxil (by GSK,) Vioxx (by Merck), Prozac (by Lilly), Augmentin (by GSK), Norvasc (by Pfizer), Zyprexa (by Lilly) EPO (by Amgen), Cipro (by Bayer), Lotrel (by Novartis), Topamx (by Johnson and Johnson), Glucotrol XL (by Pfizer), Claritin (by Schwiring), Wellbutrin SR (by GSK), Difucan (by Pfizer), Prilosec/Nexium (by Astra Zenica), Accupril (by Pfizer), Zofran (by GSK), Zithromax (by Pfizer), Imitrex (by GSK), Fosamax (by Merck) Zytrec (by Pfizer), Neurontin (by Pfizer), Pravachol (by BMS), Depakote (by Abbott). Some embodiments of the invention include two or more of the just mentioned drugs combined in a single delivery apparatus, while other embodiments of the invention include only one of the just mentioned drugs combined with another pharmaceutical and/or nutricutical and/or other substances, such as, by way of example and not by way of limitation, one or more of the pharmaceuticals and/or nutraceuticals and/or other substances listed in Appendix I. Still further, some embodiments of the invention include two or more of the pharmaceuticals and/or nutraceuticals and/or other substances listed in Appendix I in a single delivery apparatus. In this regard, the present invention includes an apparatus and a method for delivering a plurality of the medicaments listed in Appendix I for management of co-morbid diseases, illnesses, and/or conditions, as would be understood by one of ordinary skill in the art furnished with the teachings of the present invention.

[0056] It is further noted that a singe delivery apparatus, to deliver a plurality of medicaments for management of co-morbid diseases, illnesses or conditions according to the present invention may include a deliver apparatus as is disclosed in U.S. Application Serial No. 10/369,427, filed February 18, 2003, entitled "MULTI-PHASE, MULTI-COMPARTMENT CAPSULAR DELIVERY APPARATUS AND METHODS

FOR USING SAME," the contents of which are hereby incorporated by reference in their entirety; U.S. Application Serial No. 10/368,951, filed February 18, 2003, entitled "PROCESS FOR ENCAPSULATING MULTI-PHASE, MULTI-COMPARTMENT CAPSULES," the contents of which are hereby incorporated by reference in their entirety; U.S. Application Serial No. 10/369,244, filed on February 18, 2003, and entitled "MULTI-PHASE, MULTI-COMPARTMENT CAPSULAR DELIVERY APPARATUS FOR THERAPEUTIC COMPOSITIONS AND METHODS FOR USING SAME" the contents of which are hereby incorporated by reference in their entirety; U.S. Application Serial No. 10/369,247, filed February 18, 2003, and entitled "PROCESS FOR ENCAPSULATING MULTI-PHASE, MULTI-COMPARTMENT CAPSULES FOR THERAPEUTIC COMPOSITIONS," the contents of which are hereby incorporated by reference in their entirety; and PCT/US/03/10816 filed April 09, 2003, and entitled "MULTI-PHASE, MULTI-COMPARTMENT CAPSULAR SYSTEM", the contents of which are hereby incorporated by reference in their entirety, the apparatus delivering these pharmaceuticals and/or nutraceuticals and/or other substances containing them in a common phase (e.g., all solid, all liquid, etc.), or in a multi-phase (e.g., one substance solid and one substance liquid; two substances solid and one substance liquid, etc.) state as disclosed in the just mentioned references.